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**BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES**

Application Number: 09/606,977

Filing Date: June 28, 2000

Appellant(s): BYRUM, JOSEPH R.

Thomas E. Holsten
David R. Marsh
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed 3/14/05.

(1) *Real Party in Interest*

A statement identifying the real party in interest is contained in the brief.

(2) *Related Appeals and Interferences*

A statement identifying the related appeals and interferences which will directly affect or be directly affected by or have a bearing on the decision in the pending appeal is contained in the brief.

(3) *Status of Claims*

The statement of the status of the claims contained in the brief is correct.

(4) *Status of Amendments*

No amendment after final has been filed.

(5) *Summary of Claimed Subject Matter*

The summary of invention contained in the brief is correct.

(6) *Grounds of Rejection to be Reviewed on Appeal*

The appellant's statement of the grounds of rejection to be reviewed on appeal in the brief is correct.

(7) *ClaimsAppealed*

The copy of the appealed claims contained in the Claims Appendix to the brief is correct.

(8) *Prior Art of Record*

Tikhonov et al., PNAS, 96(13):7409-7414, 22 June 1999

(9) *Grounds of Rejection*

The following ground(s) of rejection are applicable to the appealed claims:

A:

Claims 2-3 and 6-7 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Claims 2-3 and 6-7 have been amended to indicate that the nucleic acid molecule according to claim 1 “further comprises” an additional element. None of the portions of the specification pointed to provide support for these concepts.

Original claim 2 recited the “substantially purified nucleic acid molecule according to claim 1, wherein said nucleic acid molecule comprises a microsatellite sequence.” As amended claim 2 recites the “substantially purified nucleic acid molecule according to claim 1, wherein said nucleic acid molecule further comprises a microsatellite sequence.” Claim 1 is directed to a substantially purified nucleic acid molecule. In the embodiment where the nucleic acid molecule of claim 1 is the complete sequence of SEQ ID NO: 1, original claim 2 is interpreted to mean that SEQ ID NO: 1 itself contains a microsatellite sequence. This seems to be the intent of the specification (see at least page 1518-1519, bridging sentence, of the specification). Original claim 2 is not interpreted to mean that a microsatellite sequence in addition to SEQ ID NO: 1 is present in the nucleic acid molecule. This concept is embraced by amended claim 2 and the specification does not appear to contemplate this. According to this interpretation, the amended claims would fairly encompass a sequence fully containing SEQ ID NO: 1 with an additional and unrelated microsatellite sequence (claim 2), with an additional and unrelated region containing a single nucleotide polymorphism (claim 3), and with an additional and unrelated promoter or partial promoter region (claim 6). The amended claims would embrace combinations of these as

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well. The examiner has only been able to find contemplation of where SEQ ID NO: 1 or a fragment thereof has these characteristics. This is not what the claims are directed to. The specification does not contemplate such nucleic acid molecules.

Claims 3 and 6-7 are considered to be new matter for the same reasons.

B:

Claims 1-7 and 20-24 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific, substantial, and credible asserted utility or a well established utility.

The sequence listing identifies SEQ ID NO: 1 as a 280 nucleotide DNA sequence with at least one wild-card nucleotide position from *Zea mays*. Table A on page 18 indicates that SEQ ID NO: 1 corresponds to clone ZM_001_A1_A01 with SEQ ID forward as ZM_001_A1_A01_T7C. These designations are not further explained.

There does not appear to be a direct assertion as to how to use SEQ ID NO: 1. There do not appear to be any particular functional characteristics of the sequence identified. While the specification generally states that SEQ ID NOS: 1-82359 encode proteins (see page 10, lines 12-16), the specification also states that SEQ ID NOS: 1-82359 are promoters (see page 11, lines 7-9) and that SEQ ID NOS: 1-82359 are markers (see page 12, lines 16-18). These are mutually exclusive classes of nucleotide sequences. For example, promoters do not encode proteins. As such, the specification does not fairly identify what SEQ ID NO: 1 is and as such, the specification cannot be considered to disclose how to use it without confirming any one of these uses or identifying an undisclosed use. Note that the specification does not disclose an open

reading frame for SEQ ID NO: 1 nor is one apparent. Note that the specification does not disclose that SEQ ID NO: 1 is a repetitive sequence in *Zea mays* that has been shown to be a marker of any trait. SEQ ID NO: 1 does not appear to share significant structure with any known marker of *Zea mays*. Note that the specification does not disclose a promoter activity for SEQ ID NO: 1 with respect to any encoded protein. SEQ ID NO: 1 does not appear to share significant structure with any known promoter. Appellant has repeatedly declined to identify which of these classes, if any, SEQ ID NO: 1 belongs to. As the functional identity of SEQ ID NO: 1 speaks to an evaluation of its utility and how to use it, appellant has been deliberately obstructive and misleading in their responses. (See for example, response filed 1/7/03 at page 5.) If SEQ ID NO: 1 is or includes a promoter, then those utilities disclosed particular to promoters would be germane. However, if SEQ ID NO: 1 encodes a protein, then those utilities disclosed particular to proteins would be germane. The examiner can only conclude that appellant has not identified what SEQ ID NO: 1 is and that the disclosure in the specification is at best misleading and at worst incorrect.

Utility of the claimed nucleic acid molecules must be evaluated as though SEQ ID NO: 1 is an uncharacterized piece of DNA.

The asserted uses for an uncharacterized piece of DNA are not a specific, substantial, and credible utility nor a well known utility. These uses are methods where the claimed invention is, itself, an object of scientific study.

C:

Claims 1-7 and 20-24 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific, substantial, and credible asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

The uses asserted for the claimed invention are methods where the claimed invention is, itself, an object of scientific study. The specification cannot enable or tell how to use the invention within 35 U.S.C. 112, first paragraph, if there is no patentable utility within 35 U.S.C. 101. The examiner maintains that there is no patentable utility for the claimed invention for the reasons set forth above and thus the claims are not enabled.

D:

Claims 23-24 are rejected under 35 U.S.C. 102(a) as being anticipated by Tikhonov et al. (PNAS, 96:7409-7414, 22 June 1999) in view of GenBank Accession No. AF123535. Tikhonov et al. discloses sequencing and analyzing regions of the maize genome. Bacterial artificial chromosomes and *E. coli* were used. GenBank Accession No. AF123535 is referenced for all sequences. (See at least abstract; page 7409, section on materials; Figure 1; and page 7411, section on analysis of the Maize region.)

Genbank Accession No. AF12535 discloses a nucleotide sequence from *Zea mays*. In particular, nucleotides 57344-57428 have significant similarity to nucleotides 196-280 of SEQ ID NO: 1. See attached alignment. For example, the 14 nucleotides GAG TTC CTC GGC TC match exactly (100% identity with this subsequence). The 42 nucleotides CCG GAG GCG TAA GAG TTC CTC GGC TCG GTC GGG CTT GCC CCT have complementarity with five

mismatches (> 90% identity with this subsequence). The use of the article “a” includes the recited identity with subsequences of SEQ ID NO: 1. The language “a” nucleic acid sequence embraces a subsequence of SEQ ID NO: 1 and the sequence of AF123535 has 100% identity with at least the particular 14mer subsequence of Tikhonov et al. “Having” and “has” are viewed as open. That is, the substantially purified nucleic acid molecule comprises a subsequence of SEQ ID NO: 1. Claims 23-24 are considered to include sequences that contain subsequences with 90%-100% identity with subsequences of SEQ ID NO: 1.

(10) Response to Argument

A:

Applicant disagrees with the examiner’s interpretation of the original and amended claims. Again the text at least at pages 1518-1519, bridging sentence, of the specification states that SEQ ID NO: 1 CONTAINS these elements and not that the elements are in addition to SEQ ID NO: 1. “Microsatellites can be observed in SEQ ID NO: 1...” “Microsatellites typically include a 1-6 nucleotide core element within SEQ ID NO: 1...”) Note that the argued utility for the polynucleotides is that SEQ ID NO: 1 contains a microsatellite sequence, single nucleotide polymorphism, or promoter.

The amended claims would fairly encompass a sequence fully containing SEQ ID NO: 1 with an additional and unrelated microsatellite sequence (claim 2), with an additional and unrelated region containing a single nucleotide polymorphism (claim 3), and with an additional and unrelated promoter or partial promoter region (claim 6). The amended claims would embrace combinations of these as well.

Contemplation of these particular embodiments is not seen in any of the portions of the disclosure pointed to by appellant. The examiner has only been able to find contemplation of where SEQ ID NO: 1 or a fragment thereof has these characteristics as set forth above. This is not what the claims are directed to. The specification does not contemplate such nucleic acid molecules.

B and C:

The examiner agrees that the “The threshold of utility is not high: An invention is ‘useful’ under section 101 if it is capable of providing some identifiable benefit,” with the proviso that the benefit be “identifiable” in the original disclosure either as a specific assertion or being readily apparent from the disclosure (i.e. well established). The examiner also agrees “the invention must have specific, i.e. not vague or unknown benefit” and “must provide a real world, i.e. practical or substantial, benefit.”

The brief does not dispute that no open reading frame (ORF), no encoded protein, nor any biological activity for any encoded protein has been disclosed for SEQ ID NO: 1. Nor has SEQ ID NO: 1 been specifically identified as containing any particular promoter, polymorphism, or microsatellite marker element.

Appellant argues that the claimed nucleic acid molecules can be used to detect the presence and/or identity of polymorphisms, as hybridization probes for expression profiling, as antisense inhibitors by introduction of the claimed nucleic acid molecules into a plant or plant cell where the resulting cell or plant is to be used to screen compounds such as herbicides, to measure the level of mRNA in a sample, and as a molecular marker. The Examiner maintains that further research is required for such uses.

Use as antisense inhibitors would require further experimentation to determine the target of inhibition. These targets are not disclosed in the specification. Appellant's arguments with respect to cell based assays are not persuasive. MPEP 2107 states, "An assay that measures the presence of a material which has a stated correlation to a predisposition to the onset of a particular disease condition would also define a "real world" context of use in identifying potential candidates for preventive measures or further monitoring." The instant specification sets forth no such correlation for any condition. It is noted that this section of the MPEP goes on to state that:

On the other hand, the following are examples of situations that require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use and, therefore, do not define "substantial utilities":

- (A) Basic research such as studying the properties of the claimed product itself or the mechanisms in which the material is involved;
- (B) A method of treating an unspecified disease or condition;
- (C) A method of assaying for or identifying a material that itself has no specific and/or substantial utility;
- (D) A method of making a material that itself has no specific, substantial, and credible utility; and
- (E) A claim to an intermediate product for use in making a final product that has no specific, substantial and credible utility.

All of these situations more closely match appellant's disclosed uses. They do not define substantial utilities.

Footnote 3 on page 11 of the brief states discusses uses of microarrays. Appellant is not claiming microarrays or collections of nucleotides and the specification does not associate any of the claimed sequences with any trait of interest. Contrary to appellant's assertions, further experimentation is required to identify a "real world use." A negative result to such a screen tells what the nucleic acid is not and cannot be used for. A positive result to such a screen requires further experimentation to determine what, if anything, such a change means. It is not an

immediate benefit except in the sense to indicate that further research might yield a "real world use."

The brief on page 12-13 discusses gas chromatographs. MPEP 2107 in discussing research tools sets forth the following:

Some confusion can result when one attempts to label certain types of inventions as not being capable of having a specific and substantial utility based on the setting in which the invention is to be used. One example is inventions to be used in a research or laboratory setting. Many research tools such as gas chromatographs, screening assays, and nucleotide sequencing techniques have a clear, specific and unquestionable utility (e.g., they are useful in analyzing compounds). An assessment that focuses on whether an invention is useful only in a research setting thus does not address whether the invention is in fact "useful" in a patent sense. Instead, Office personnel must distinguish between inventions that have a specifically identified substantial utility and inventions whose asserted utility requires further research to identify or reasonably confirm. Labels such as "research tool," "intermediate" or "for research purposes" are not helpful in determining if an applicant has identified a specific and substantial utility for the invention.

Again, further experimentation is required to use determine and confirm any of the uses set forth by appellant for the claimed nucleotide sequences.

The gas chromatograph example set forth by appellant, particularly as discussed in Footnote 5 on page 12, is not analogous to the present disclosure. A gas chromatograph is a piece of equipment designed and built for a particular use. Such equipment is fully tested, evaluated, and calibrated to ensure accurate results. Those skilled in the art use gas chromatographs to analyze both known and unknown compounds. When the compound is unknown, the results obtained are compared to results for known compounds, e.g. standards. Appellant did not design the claimed nucleotide sequences for any particular purpose. They merely isolated them. They have not tested, evaluated, or calibrated the claimed nucleotide sequences for any particular use. Sampling for the presence or absence of chlorine in a crude oil sample is not analogous to the present situation. The presence or absence of chlorine in a crude

oil sample has a known meaning based upon prior research. Absent establishment of this association between presence of chlorine and destruction of catalyst, the presence or absence of chlorine in a sample would not provide any useful information to the refinery manager. Likewise, the presence or absence of any of the claimed nucleotide sequences in a sample (or polymorphisms thereof) has no meaning absent some association. Further experimentation is required to determine what that meaning or association might be.

In addition, this gas chromatograph analogy fails address appellant's own definition of the term polymorphism. The specification (page 1564, lines 1-5) defines "polymorphism" as "a variation or difference in the sequence of the gene or its flanking regions that arises in some members of a species." It follows from this definition that if there is no "variation or difference in the sequence of the gene or its flanking regions" among "members of a species," then no polymorphism exists, i.e. a polymorphism is absent, in this region of the genome. A "polymorphism" is a collective concept defined by at least two variants (or alleles) found within members of a species collectively. Thus, one detects the *presence* of a polymorphism by analyzing multiple members of the species, i.e. analyzing a population. While one can detect the absence (or presence) of a specific allele of the polymorphism in a specific individual member of the species, one cannot detect the *absence* of a polymorphism *per se* based on one individual alone. The absence of a particular allele necessarily means that a different allele is present. The specification fails to disclose a specific and substantial utility for the claimed invention in the capacity of detecting polymorphisms, because it does not disclose whether the claimed nucleic acid molecules can, in fact, be used to detect any polymorphism whatsoever. Thus, the specification leaves open the possibility that there may be no polymorphism to detect. With

respect to the gas chromatograph analogy, one can only detect the absence of a compound, such as chlorine, in a sample, *if* it was already known that chlorine could, in fact, be detected by the gas chromatograph were it present in the sample.

The specification generally teaches using the claimed polynucleotides to identify a polymorphism, but fails to teach that a polymorphism could in fact be detected, or a specific polymorphism that could be detected. The specification generally teaches using a polymorphism, detectable with the claimed nucleic acid molecules, as a molecular marker for a linked trait of interest, but fails to teach either the polymorphism or the trait of interest. The court in *Kirk* (at page 53) held:

We do not believe that it was the intention of the statutes to require the Patent Office, the courts, or the public to play the sort of guessing game that might be involved if an applicant could satisfy the requirements of the statutes by indicating the usefulness of a claimed compound in terms of possible use so general as to be meaningless and then, after his research or that of his competitors has definitely ascertained an actual use for the compound, adducing evidence intended to show that a particular specific use would have been obvious to men skilled in the particular art to which this use relates.

The specification (page 1564, lines 1-5) defines “polymorphism” as “a variation or difference in the sequence of the gene or its flanking regions that arises in some members of a species” (emphasis added). The following pages of the specification discuss various types of sequence polymorphisms and how they are detected. It is noted that on page 1567, line 17, the specification states, “By correlating the presence or absence of it [a polymorphism] in a plant with the presence or absence of a phenotype...” Thus, the specification acknowledges that further analysis is required to determine a use for a polymorphism even assuming one is found. A change of phenotype and correlation with phenotype must be found; linkage analysis must be performed.

Even to determine whether a polymorphism exists at a specific chromosomal location requires hybridization to at least two individual chromosomes, and generally involves analyzing genomic DNA from multiple members of a species; the specification discloses no such analysis. The specification fails to disclose: 1) whether the claimed nucleic acid molecule can in fact detect a polymorphism, or even whether such a polymorphism exists; and 2) at least one specific example of at least one of the types of polymorphisms described in the specification. The specification does not disclose any utility in this context for a nucleic acid molecule or EST that can NOT detect a polymorphism. Therefore, using the claimed invention to first determine whether or not the claimed nucleic acid molecule can, in fact, detect a polymorphism *is* to determine whether or not the claimed invention has a utility that requires detecting a polymorphism, i.e. it is “use testing” and not substantial. Since the specification fails to identify even one specific polymorphism that can be detected with the claimed nucleic acid molecule, the specification fails to show any specific correspondence between the disclosed general utility and the claimed subject matter, regardless of any specific application requiring detection of polymorphisms.

Appellant argues that the claimed nucleic acid molecules have utility as “probes for other molecules or as a source of primers.” In particular, to use the claimed nucleic acid molecules to find the promoter of the corresponding gene or to initiate a chromosome walk. The argument in the brief compares the claimed invention to a microscope.

A microscope is useful for determining structure of *any* sample of interest at the macroscopic, microscopic or molecular level, depending on the type of microscope. It is a generally useful tool for a wide range of specific uses. One does not usually use a microscope to

study related microscopes. In contrast, appellant argues that the claimed nucleic acid molecules are useful to detect or measure nucleic acid molecules that possess a certain level of structural relatedness to the claimed nucleic acid molecules, the level of relatedness being defined by hybridization to the claimed nucleic acid molecules. However, the specification discloses *no* nucleic acid molecule that hybridizes with the claimed nucleic acid molecules that does *not* consist or comprise SEQ ID NO: 1 or its complement. In order for hybridization between two nucleic acid molecules to occur, they must share at least some nucleotide sequence that is fully complementary. The length of fully complementary sequence required to detect hybridization depends primarily on the stringency of the specific hybridization conditions employed, the lower the stringency the shorter the length of fully complementary sequence required. The specification also fails to disclose any hybridization conditions required for detecting nucleic acid molecules that do *not* contain the nucleotide sequence of any of SEQ ID NO: 1 or its complement (other than subsequences of SEQ ID NO: 1), in addition to failing to disclose any source for such nucleic acid molecules.

All arguments pertaining to the utility of the claimed invention with respect to studying the corresponding genomic DNA and mRNA found in maize or corn, would also apply to any homologous nucleic acid molecules found in other plant species. In so much as the specification fails to describe a specific and substantial utility for the corresponding nucleic acids in maize or corn, so does it fail to describe a specific and substantial utility for the corresponding nucleic acids in other plant species.

Appellant cites *Carl Zeiss Stiftung v. Renishaw PLC* in support of their position that utility has been established. However, this decision is with respect to a mechanical device and

not a laboratory reagent or research tool. Furthermore, appellant mischaracterizes the findings in this decision. This decision concerned claim interpretation and the CAFC found that the district court had erred in their interpretation of what the claim embraced and thus what was required to establish utility. The claimed device was found to fulfill the stated objective of mounting a stylus by the CAFC. These facts do not correspond to the instant specification.

While the specification teaches (page 1563, lines 1-7) that the claimed nucleic acid molecules “*can be used* … to isolate molecules from other cereals” (emphasis added), the specification does not indicate that any such nucleic acid molecules *had been* obtained, nor does it describe any characteristics possessed by such nucleic acid molecules. As to whether such molecules could, in fact, be obtained, the Office can neither prove nor disprove the assertion because the Office does not have laboratory facilities. At the time the application had been filed, future experimentation on the part of one skilled in the art would have been required to determine which, if any, other plant species contained nucleic acid molecules that could have been obtained using the claimed invention, and under what experimental conditions.

With respect to using the claimed nucleic acid molecules to initiate a chromosome walk, such as to isolate a promoter of the corresponding gene, the specification fails to disclose any characteristics of the corresponding promoter, or any other promoter within “chromosome walking” distance; neither structural characteristics, by which the promoter might be identified, nor functional characteristics, by which a specific and substantial use for the promoter might be determined.

In this context, the claimed invention does not compare to a golf club, because one knows what a golf ball is and how to use the golf club to hit it, whereas the specification does not

disclose or describe with particularity any known useful nucleic acid molecule that can be obtained, such as the corresponding promoter - it simply invites the skilled artisan to provide such information by further experimentation.

Even assuming *arguendo* that the corresponding promoter exists is no more guidance for its isolation, and eventual use, than knowing that a haystack contains a needle - at least one is presumed to know what the needle looks like. Also, the specification does not disclose the distance or direction one has to walk on a chromosome from the corresponding location to reach the corresponding promoter. Thus, starting the walk at the corresponding chromosomal location is no more help in identifying the promoter than is picking a specific location in a haystack to start looking for a needle when one does not know where the needle is relative to the starting location. Initiation of a chromosome walk at the corresponding chromosomal location is considered non-specific because any EST would serve the purpose for isolating an uncharacterized promoter, since any chromosomal location is expected to be linked to a promoter. The specification fails to disclose sufficient characteristics of the corresponding promoter, such as its sequence or precise location relative to the genomic location corresponding to the claimed nucleic acid molecule, to inform one of what the corresponding promoter is or when it has been isolated. For example, a nucleotide sequence is identified during the chromosome walk as a putative promoter by sequence analysis, is then subcloned into operable linkage with a reporter gene and transfected into an appropriate cell, but found not to express the reporter gene in the cells. This result could mean the putative promoter: is not truly a promoter, i.e. a false positive; is not the corresponding promoter; or is incomplete, i.e. lacked additional sequence elements required for promoter activity in the seed pod cells. Substantial utility means

that “one skilled in the art can use a claimed discovery in a manner which provides some *immediate* benefit to the public,” *Nelson v. Bowler*, 206 USPQ2d 881, 883 (CCPA 1980) (emphasis added). Since the specification does not describe the corresponding promoter, or any other specific nucleic acid molecule, sufficient to inform one skilled in the art that it has been isolated, there can be no “*immediate* benefit to the public” in using the claimed nucleic acid molecule in this capacity; “a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion,” *Brenner* at page 696.

With respect to the “real world” value of ESTs in general (brief, pages 15-17), it is asserted that there is “no question that the public has recognized the benefits provided by the claimed subject matter, and has attributed ‘real world’ value to such nucleic acid molecules.” It is unclear as to what evidence appellant is alluding. The evidence supplied by appellant shows that a multimillion dollar industry has arisen surrounding buying and selling EST databases and clones, not that anyone in this industry has bought or sold the claimed subject matter. It is further noted that this industry is presently in decline as evidenced by companies laying off large portions of their work force as well as moving away from EST data as their core business. It is noted that simply because a product, such as an EST sequence database or clone library, is bought and sold does not mean it has patentable utility.

With respect to credibility, appellant is reminded that in order to meet the requirements of 35 USC 101, the specification must disclose at least one utility that is specific and substantial, as well as credible (absent a showing of well established utility, which would presume that the utility was credible). The claims have been rejected because 1) the specification fails to disclose at least one utility that is both specific and substantial, and 2) no convincing evidence has been

presented to show that an EST, for which only its nucleotide sequence and source have been disclosed, has a well established utility.

The examiner maintains that the uses asserted for the claimed invention are methods where the claimed invention is, itself, an object of scientific study, e.g. to determine whether the corresponding genomic DNA of maize or corn contains a polymorphism that can be detected with the claimed invention. The specification cannot enable or tell how to use the invention within 35 U.S.C. 112, first paragraph, if there is no patentable utility within 35 U.S.C. 101. The examiner maintains that there is no patentable utility for the claimed invention for the reasons set forth above and thus the claims are not enabled.

Insofar as the specification fails to describe a specific, substantial, and credible utility for SEQ ID NO: 1 itself, so does it fail to describe a specific and substantial utility for the nucleic acid molecules that hybridize to SEQ ID NO: 1 (see for example claim 1), are complementary to SEQ ID NO: 1 (see for example claim 1), contain additional elements (see for example claims 2-3 and 5-7), are fragments of SEQ ID NO: 1 (see for example claim 21), or have a level of similarity with SEQ ID NO: 1 (see for example claim 23). This is particularly true for those utilities such as use as probes or use as markers as these sequences have only limited identity to the naturally occurring sequence.

D:

Claims 23-24 are considered to include sequences that contain subsequences with 90%-100% identity with subsequences of SEQ ID NO: 1. Tikhonov et al. discloses such sequences in Genbank Accession No. AF123535.

For the above reasons, it is believed that the rejections should be sustained.

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Respectfully submitted,

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mpa
May 26, 2005

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AF123535
LOCUS AF123535 160480 bp **DNA** linear **PLN** 19-MAR-2000
DEFINITION Zea mays alcohol dehydrogenase 1 (adh1) gene, adh1-F allele, complete cds.
ACCESSION AF123535
VERSION AF123535.1 **GI**:7262818
KEYWORDS
SOURCE
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Eukaryota; Viridiplantae; Streptophyta; Embryophyta; Tracheophyta; Spermatophyta; Magnoliophyta; Liliopsida; Poales; Poaceae; PACC clade; Panicoideae; Andropogoneae; Zea.
REFERENCE 1 (bases 1 to 160480)
AUTHORS Tikhonov,A.P., SanMiguel,P.J., Nakajima,Y., Gorenstein,N.M., Bennetzen,J.L. and Avramova,Z.
TITLE Colinearity and its exceptions in orthologous adh regions of maize and sorghum
JOURNAL Proc. Natl. Acad. Sci. U.S.A. 96 (13), 7409-7414 (1999)
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REFERENCE 2 (bases 1 to 160480)
AUTHORS SanMiguel,P.J., Tikhonov,A. and Bennetzen,J.L.
TITLE Direct Submission
JOURNAL Submitted (25-JAN-1999) Biological Sciences, Purdue University, Hansen LSRB, Rm. 339, West Lafayette, IN 47907, USA
FEATURES
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BASE COUNT 42638 **a** 37287 **c** 36880 **g** 43550 **t** 125 **others**
ORIGIN

June 2d,
1999

Query Match 18.4%; Score 51.4; DB 8; Length 160480;
Best Local Similarity 75.3%; Pred. No. 5.1e-06;
Matches 64; Conservative 0; Mismatches 21; Indels 0; Gaps 0;

Qy 196 tgagtgccttcggaaaggtagcggacttgcgtatctgtatccggaggcgtaagagtt 255
Db 57344 TGGGTCACTTTCTGTCGGGGTGATGAGTGAGGTGTCCTAACCCGGAGGCATAGGAGTT 57403

Qy 256 cctcggtcggtcggtcccct 280
Db 57404 CCTCGGCTCAGTCGGCCTCGCCACT 57428